

REMARKS/ARGUMENTS

I. Status of Claims

Claim 1 is amended.

Claims 2, 18, and 19 were previously canceled.

Claims 3-9, 13-17 and 20-47 were previously withdrawn.

Claims 1 and 10-12 are being examined.

Support for the claim amendments are found through out the specification, see for example, pp. 11-13, and original claims as filed.

II. Objections to Claims 3 and 9.

On page 3 of the Office Action, the examiner objected to claims 3 and 9 as being improperly dependent. Applicants note that claims 3 and 9 were previously withdrawn and therefore not subject to the present examination. Upon allowance of claims 1 and 10-12, applicants will timely cancel all withdrawn claims.

III. Claims 1 and 10-12 Satisfy 35 U.S.C. §112 2nd Paragraph Requirements

On page 3 of the Office Action, the examiner rejected claim 1 under 35 U.S.C. §112 2nd paragraph because the examiner alleges that “it is unclear whether the dashes on the left side of A₁ and the right side of NH in the compound or [*sic*] formula (Ic) are intended to describe a bond or a methyl group”.

As previously stated by the applicants, the compound embodied by (Ic) is a “partial structure” and therefore the dashes inherently represent a linkage/bond. Support for this is found for example on p. 11, first paragraph, p.33, line 1 to p. 35, line 3, claims 3, 11, and 12 as originally filed. Nevertheless, to expedite prosecution, claim 1 is amended to expressly state that the dash is a bond.

Therefore, the applicants request §112 rejections over claims 1 and 10-12 be withdrawn.

IV. Claims 1 and 10-12 are Not Obvious Over Rehmer et al., (U.S. Pat. No. 5,073,611) under 35 U.S.C. §103(a).

On page 5 of the Office Action, the examiner states “the claimed spacers are so closely related structurally to homologous compounds of the reference as to be structurally obvious there in the absence of any unobviousness or unexpected properties...”.

Applicants previously argued that Rehmer et al. neither describes nor suggests the composition of claims 1 and 10-12. The amended structure (Ie) of claim 1 has a minimum of 4 additional $-\text{CH}_2\text{CH}_2\text{O}-$ unit (when r is 4) over Compound B1 of Rehmer. Applicants state that the additional $-\text{CH}_2\text{CH}_2\text{O}-$ units offer additional length for the spacer and may also play a role in the hydrophilic/hydrophobic balance of the attaching moieties, as demonstrated by Tamura et al. (2003), discussed *infra*. While, the examiner did not provide any evidence to show that Compound B1 of Rehmer that differs from the claimed structure possesses similar property other than mentioning that the structures are “generally of sufficiently close structural similarity”, the applicants herein provide objective evidence of unexpected properties.

Applicants herein submit a peer-reviewed journal publication by Tamura et al., (2003), *Bioconjugate Chem.* 14: 1222-1230, that demonstrates that a suppressive effect on non-specific binding is not sufficient when r is small as in the monomer of the cited reference. A copy of the publication is enclosed herewith. The monomer of Rehmer et al. is similar to $n=0$ in Tamura et al. The claimed structure is similar to the $n=1-2$ in Tamura et al. The Fig. 5 of Tamura et al. demonstrates that the non-specific binding of tubulin and actin proteins is significantly suppressed when $n=1$ or more as compared to $n=0$, while the binding specificity of the target protein (*i.e.*, FKBP12) was nearly constant. Thus, Tamura et al. shows that the amount of nonspecific protein binding proteins decreased in proportion to the number of spacer monomers while that of the target protein, FKBP12, was essentially constant. This result was unexpected because there is no evidence in Rehmer that increasing the spacer length would result in selective suppressing of the non-specific binding of the proteins whereas, the binding efficiency of the desired target protein remains the same. Therefore, the unexpected suppressing of the undesirable binding of non-specific proteins alone in the absence of a similar reduction for the specific protein, due to the increase in the number of spacers, demonstrates that the claimed structure is non-obvious over Rehmer et al.

Applicants request withdrawal of the §103(a) rejection over Rehmer et al., and move the pending claims to allowance.

No other fees are due. However, please charge any fees that might be due in connection with this submission to our Deposit Account No. 12-0913 with respect to our matter number 43512-104208.

Respectfully submitted,

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